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RESEARCH ARTICLE

PHARMACOLOGICAL SIGNIFICANCE OF *MANGIFERA INDICA* IN OVERCOMING PAIN AND IMPROVING LIFE

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ABSTRACT

Background: No matter how advanced the world is today, working for this advancement and high standards of life always comes with pain. Since the evolution of humankind, people have been using different products of natural origin for pain management because of their effectiveness and fewer side effects. **Objective:** The main objective of the current study was to extract the fruit pulp of *Mangifera indica* and investigate its pharmacological impact. **Methodology:** Different dosages were evaluated, including 250 and 500 mg/kg of the plant extract. The hot plate method, tail flick, and writhing tests were used to estimate analgesic activity. Carrageenan-induced paw edema was performed to determine the anti-inflammatory response. **Results**: The obtained data revealed significant activity at 250 mg/kg and highly significant activity at 500 mg/kg via the hot plate method for evaluation. In the tail-flick test, extract at both doses exhibited highly considerable activity. In the writhing test, the maximum inhibition of writhes was observed at a dose of 500 mg/kg, with the number of writhes decreasing from 22 to 11 within 20 minutes, resulting in an inhibition rate of 49.36%. For the carrageenan test, both doses exhibited substantial inhibition outcomes on the mean increase in paw volume for the different periods. Maximum inhibition was observed during the 5 hours of time intervals with 35.74% and 37.85% of doses. **Conclusion:** The results suggest that *Mangifera indica* possesses significant medical importance and could be used for therapeutic purposes.

Keywords: Analgesic activity, Hot plate test, *Mangifera indica*, Tail flick test, Writhing test

INTRODUCTION

Following the International Association for Study of Pain (IASP), pain can be described as an *"Unpleasant sensory or emotional experience related to actual or potential injury to tissue"*. This definition provides the basis for varying aspects of underlying pain physiology (1). The reorganization of stimuli responsible for the injury to the tissue exhibited a crucial impact on the determination of behavioral processes. Nociception contributes substantially to the initiation of pain, and an individual may undergo a complex sensory process of pain without pronounced activity. The mechanism of nociception is regulated mainly by nociceptors. The stimuli that cause the tissue injury are termed noxious stimuli, which are triggered by different factors, depending upon whether they are chemical or mechanical, resulting in the initiation of nerve signals that are perceived as pain by the brain. Although pain is protective and essential for survival, it is also a great source of discomfort.

Based on a diverse array of characteristics, pain can be classified into three general classes, namely, nociceptive, inflammatory and pathological pain. This type of pain can be more broadly categorized as neuropathic or dysfunctional. Pain pathways are divided into three stages: conduction, transmission, and modulation (2, 3). For pharmacological therapy, NSAIDs have been primarily used in pain treatment and management, along with steroidal anti-inflammatory agents and opioids. All these therapies are associated with adverse effects, enduring more harmful impacts on the health of an individual, such as in the case of NSAIDs, gastrointestinal upset, and renal insufficiency. People treated with opioids may undergo drug dependence and respiratory depression (4).

Substances isolated from natural sources have been involved in the promotion of better health benefits for ages. People from different civilizations have been using natural products to treat diverse diseases. Herbal remedies have been contributing to the healthcare system for a long duration. Many medicinal plants open the way for discovering natural products with potential medicinal characteristics. In addition, it has been estimated that 25% of the medicinal formulations originate from plants. Following the WHO report, medicinal products have been utilized as medicine and for nutritional purposes, especially in undeveloped localities. The research and the development of ethnobotanicals may help in the discovery of novel compounds. Products obtained from natural sources have been the backbone for managing and treating diseases. Herbal medicines have become more popular and preferred among a wide array of people with the passage of time. They contribute a significant role in the process of evolution of a novel pharmacological product (5).

Mangifera indica, commonly known as "Mango" and "AAM" in Urdu (in the subcontinent). Its distinct medicinal characteristics are attributed to different parts. *Mangifera indica* has been of keen interest to researchers. It has been known to possess significant pharmacological properties. It has shown antioxidant, antibacterial, antidiabetic, antidiarrheal, immune-modulatory, and hepato-protective effects. It contains a wide range of phytochemicals whose composition varies among different parts. Flavonoids, triterpenoids, and polyphenolics are highly regarded (6). The essential oil obtained from *Mangifera indica* has been found to contain substances that possess antimicrobial properties, the inhibitory α glucosidase, and immunosuppressive properties are also attributed to benzophenone derivatives. The *Mangifera indica* is also a potential source of proteins, lipids, and minerals such as calcium, iron, potassium, and phosphorous (7, 8).

Mangifera indica, commonly known as the mango plant, has bioactive compounds in almost all parts of the plant, which help manage conditions like malaria, bacterial, fungal, and plasmodia infections. Such characteristics in any commonly used fruit are so beneficial and cost-friendly to be used instead of expensive classical and modern drugs. The plant also helps to treat infections in the oral cavity. The plant also contains anti-inflammatory and immune-modulatory properties (9, 10). The current study was planned to explore the analgesic effect of the plant as it has not been

studied in many past studies.

METHODOLOGY

Preparation of extract

The fresh extract of *Mangifera indica* was prepared from fruit pulp. The pulp was soaked in 8 litres of ethanol for two weeks and stored in an oven at 40°C. Then, the mixture was passed through the Whatman filter paper and passed through a rotary evaporator (BUCHI Rotavapor R-200). The semisolid mass obtained was subjected to the process of freeze drying.

Animals

Swiss Albino mice and rats of both sexes weighing from 25-30 g and 160- 210 g were taken from the animal house facility of the University of Karachi, Pakistan. Throughout the experiment, a constant environment has been maintained. The animal studies were performed following the National Institute of Health guidelines for the care and use of Laboratory animals (11). All the ethical guidelines as provided by the institutional animal care review committee, were maintained during the research trials. Ethical approval for animal care has been granted by the Board of Advance Studies and Research (BASR), University of Karachi, with approval number (ERC No: 04178/Pharm).

Animals were divided into groups of seven and kept in standard conditions at a temperature of 23°C + 2 °C with 12 h of light and dark cycles. Animals were fasted overnight but were allowed fresh water and labitinum before the administration of the extract. Animals involved in any previous experiments were omitted. Animals that were fed anything except the prescribed diet were not considered.

Experimental design

The sample size was designed by randomized sampling techniques while keeping the same number in all three test groups. Animals were divided into four groups of seven animals in each test and treated as follows:

Group 1: The control group received vehicle only (Distilled Water)

Group 2: The test group received ethanolic extract of *Mangifera indica* 250 mg/kg

Group 3: The test group received ethanolic extract of *Mangifera indica* 500 mg/kg

Group 4: Standard received Disprin (aspirin) 300 mg/kg

Assessment of analgesic activity

The following tests were performed to estimate the analgesic activity of the extract.

Hot plate method

The hot plate method involves the placement of an animal on an electrically heated surface maintained at a temperature of 55±1°C. The time occupied by the mice to withdraw their tails was noted at different time intervals. The initial reading was noted before administering the vehicle, extract, and drug. The reaction interval consumed for mice was indicated at 30, 60, 90, 120, 150 and 180 min after administering vehicle, extract and standard drug (12).

Tail flick test

In the tail flick method, mice with one-third of their tails submerged in a boiling water bath were kept at 51 °C. It helps determine the latency of the withdrawal of the tail of mice. The readings were taken before and after administering water, extract, and aspirin at 0, 30, 60, 90, 120, 150, and 180 minutes (13).

Writhing test

The writhing was induced with 0.9% acetic acid. Following a 30-minute dosage, animals were placed in a clear box, and acetic acid was administered intraperitoneally. The amount of writhing that included hind leg elongation, extension, and abdominal contraction was counted (14).

1.4. Anti-inflammatory activity

Carrageenan-induced paw edema: The addition of 1% carrageenan to the hind paw's plantar surface affected inflammation. The rats were given the extract, aspirin, and vehicle treatment before receiving a carrageenan injection. The Plethysmometer (Ugo Basile) was used to measure the paw edema of rats at 0 hours, 1 hour, 2 hours, 3 hours, 4 hours, and 5 hours following the carrageenan injection (15).

Statistical analysis

All the statistical analyses were performed using ANOVA and a post-hoc Tukey test using SPSS 22. The $p<0.05$ is considered significant.

RESULTS

Analgesic effect of *Mangifera indica*

The results revealed that at 90 minutes, the effects of a 250 mg/kg dosage of *Mangifera indica* extract were substantial compared to the control. Table 1 illustrates how the effect of the extract at the other dose of 500 mg/kg decreased over time. At 30, 60, and 90 minutes, the extract was found to be more significant, highly significant at 120 minutes, and significant at 150 minutes as compared to control. In contrast, aspirin has exhibited very highly significant results at all-time intervals compared to the control. The extract has shown a more pronounced analgesic effect at both doses at 90 mins, more marked at 500 mg/kg. The tail flick method determined the anti-nociceptive activity, as shown in Table 2. The results are represented as a mean increase in latency after administration of drug±S.E.M. Compared to the control, the extract of Mangifera indica at both doses—250 mg/kg and 500 mg/kg—produces very significant outcomes at all time intervals. Notably, 90 minutes was the maximum reported reaction time to flick the tail. When compared to the control group, the mice took significantly longer to flick their tails during both doses. Results of the standard drug aspirin at a dose of 300 mg/kg are found to be very highly significant. For the acetic acid-induced writhing test, at a dose of 250 mg/kg, the extract caused a reduction in the number of writhes to 14 (38.73%), whereas, at another dose of 500 mg/kg, the number of writhes reduced to 11.57% (49.36%), as compared to mean writhes of 22.85 of control (Table 3).

Table 1. Hot plate test

Groups	Dose (mg/kg)	Reaction time (minutes)						
		Pre-drug	30	60	90	120	150	180
Control	2	8.227 ± 0.160	8.312± 0.155	8.460± 0.141	8.600± 0.083	8.438± 0.148	8.192± 0.116	7.927± 0.198
Mangifera indica	250	7.905 ± 0.182	8.464± 0.148	9.500± 0.148	11.982 ± 0.573*	10.905 ± 0.541	9.940± 0.358	8.974± 0.306
Mangifera indica	500	8.002 ± 0.154	9.317± 0.290*	10.698 ± 0.37*	13.330 ± 1.196*	12.765 ± 1.191*	10.912 ± 0.790*	9.275± 0.480
Aspirin	300	8.304 ± 0.100	11.208 ± 0.502*	14.131 ± 0.583*	16.391 ± 0.441*	15.551 ± 0.481*	14.292 ± 0.455*	13.684 ± 0.456*

*$p<0.05$ as compared to control

Table 2. Tail flick test

Groups	Dose (mg/kg)	Analgesia TFLD or mean increase in latency after drug administration (minutes)						
		Pre - drug	30	60	90	120	150	180
Control	2	0.115± 0.004	0.124± 0.006	0.132± 0.008	0.107± 0.007	0.101± 0.004	0.118± 0.005	0.107± 0.006
Mangifera indica	250	0.122± 0.017	2.717± 0.265*	2.841± 0.257*	3.738± 0.373*	3.425± 0.251*	2.654± 0.170*	2.088± 0.118*
Mangifera indica	500	0.122± 0.011*	2.795± 0.215*	3.460± 0.282*	4.487± 0.367*	4.067± 0.269*	2.977± 0.234*	2.138± 0.185*
Aspirin	300	0.114± 0.005	3.124± 0.255*	4.365± 0.436*	4.557± 0.389*	4.687± 0.355*	3.048± 0.241*	2.825± 0.237*

*p<0.05 as compared to control

Table 3. Acetic acid-induced writhing Test

Groups	Dose (mg/kg)	Mean± S.E.M	Percentage Inhibition (%)
Control	2	22.857±0.936	____
Mangifera indica	250	14.00±0.297*	38.73
Mangifera indica	500	11.571±0.202*	49.36
Aspirin	300	8.428±0.297*	63.15

*p<0.05 as compared to control

Carrageenan-induced paw edema

In the current study, at both the doses of *Mangifera indica* that are 250mg/kg and 500mg/kg, the mean values of paw edema volume (ml) are statistically very highly significant at all time intervals as compared to control results represented in Table 4. The mean values of paw edema volume of standard drug aspirin are also statistically very highly significant as compared to the control. Both doses of *Mangifera indica*, which are 250mg/kg and 500 mg/kg demonstrated substantial effects on the average paw volume over all time intervals. Maximum percentage inhibition at 250mg/kg and 500mg/kg was observed at 5h, with 35.74% and 37.85%, respectively, in contrast to the control. The standard drug aspirin showed maximum percentage inhibition at 5h, which is 62.61%, compared to the control, with significant inhibitory effects on mean increase in paw volume at all time intervals. It may be assumed that the anti-inflammatory activity of *Mangifera indica* may be due to the inhibition of prostaglandins. Maximum anti-inflammatory effects have been observed (Tables 5 and 6).

Table 4. Carrageenan–induced rat paw edema

Groups	Dose (mg/kg)	Mean paw edema volume (ml)					
		0h	1h	2h	3h	4h	5h
Control	2	2.568± 0.168	5.864± 0.328	6.764± 0.328	7.175± 0.204	7.111± 0.213	6.848± 0.237
Mangiferaindica	250	2.124± 0.105*	4.544± 0.064*	5.065+ 0.075*	5.211± 0.182*	5.125± 0.068*	4.875± 0.065*
Mangiferaindica	500	2.095± 0.105	4.437± 0.148*	4.881± 0.142*	5.11± 0.144*	5.010± 0.133*	4.751± 0.135*
Aspirin	300	2.231± 0.135	3.727± 0.290*	3.881± 0.158*	3.937± 0.017*	3.911± 0.017*	3.835± 0.0163*

*p<0.05 as compared to control

Table 5. Change in paw volume

Groups	Dose (mg/kg)	Mean increase in paw volume (ml)					
		0h	1h	2h	3h	4h	5h
Control	2	2.568	3.30+0.351	4.20±0.351	4.61±0.234	4.54±0.242	4.28±0.242
Mangifera indica	250	2.12	2.42+0.105	2.94±0.146	3.09±0.147	3.0±0.148	2.75±0.109
Mangifera indica	500	2.09	2.34+0.170	2.79±0.170	3.01±0.164	2.92±0.162	2.66±0.163
Aspirin	300	2.23	1.49+0.104	1.65±0.119	1.70±0.123	1.68±0.122	1.60±0.119

Table 6. Inhibition of paw edema

Groups	Dose (mg/kg)	Inhibition of paw edema (%)					
		0h	1h	2h	3h	4h	5h
Mangifera indica	250	17.18	26.66	30.0	32.97	33.96	35.74
Mangifera indica	500	18.35	29.09	33.57	34.70	35.68	37.85
Aspirin	300	12.89	54.84	60.71	63.12	62.99	62.62

DISCUSSION

Herbal medicines are being extensively used because of their convenience, cost-effectiveness, and fewer side effects. 75-80% of people all around the world prefer natural products for treatment due to their low side effects, especially in developing countries. W.H.O. has reported that the world's population is inclined twice towards herbal medicines in comparison with conventional therapy. Natural products form the foundation of the primary health care system. Many drugs that are now an integral part of the allopathic system of medicine originate from plant sources (16-18). With time, the search for plant-based products has been significantly increased (19).

Pain is manifested in a variety of diseases involving complications due to complex processes, inflammatory mediators, and damage to the tissue. Despite the advances in allopathic medicines, they are still associated with severe side effects ranging from gastrointestinal upset and bleeding to liver damage and much more. Safety and efficacy are among the most critical parameters in terms of the provision of medical care. Screening of medicinal plants resulted in acquiring the analogues, which produced pharmacological activity with more safety and efficacy through subjection to a proper methodology.

The result of the analgesic activity of *Mangifera indica* revealed that both doses of extract exhibited significant results in all three animal models compared to the control. In the hot plate method, there was an upsurge in the reaction period. Maximum analgesic activity at both doses was observed at 90 minutes. Assessment of analgesic activity was also carried out using the tail-flick method. It was noted that the mice flicked the tail due to pain, with the highest reaction time at 90 minutes at both doses and gradually decreasing towards 120 minutes. Another test used to determine the analgesic effect was the writhing test. The extract showed a markedly significant effect on the reduction of writhes at both doses compared to the control group. Acetic acid-induced writhing test used to check peripheral analgesic effect. The visceral pain was introduced through acetic acid. Acetic acid (0.9%) was injected intraperitoneally, releasing inflammatory factors, including histamine and bradykinin, that further stimulated nociceptive fibres. Peritoneal receptors were involved in the constriction of the abdomen (20). The extract at both doses caused inhibition of writhes.

A carrageenan-induced paw edema test was used to assess the anti-inflammatory activity at different time intervals. Carrageenan causes the subsequent release of different factors, including tumor necrosis factor-alpha–α, Interleukin 1-β, Interleukin-6, COX product, cytokines, and Interleukin-8, causing the release of sympathetic amines. Different inflammatory mediators are involved in carrageenan-induced paw oedema, marked by biphasic events. In the first phase, there is a release of different inflammatory mediators, and then in the second phase, there is a production of TNF- α, IL-1β, and IL-6 prostaglandins (21).

Mangifera indica contains various polyphenolic compounds, and their presence differs among parts (peel, pulp, stem, bark, leaves, flower). In all parts of *Mangifera indica*, polyphenols are

present, which impart significant properties. There are different significant phytochemicals present in a pulp of *Mangifera indica*, such as polyphenols, including mangiferin, gallic acid, gallo tannins, ellagic acid, quercetin, isoquercetin, β-glueogalin, flavonoids (15). Mangiferin has been found to possess potent analgesic and anti-inflammatory activity (22). Gallic acid has also been found to significantly reduce histamine release and cause the inhibition of inflammatory mediators (23). Studies have shown that they cause inhibition of some of the mediators involved in the inflammatory process (24). Quercetin also has been found to possess anti-inflammatory activity (25).

Several phytochemicals are found in different parts of *Mangifera indica*. The chief constituents are mangiferin, tannins, and gallic acid. Polyphenolics, flavonoids, and triterpenoids are also of interest (26). Different studies involving various parts of *Mangifera indica* have been performed worldwide to evaluate its significant role in several diseases. The results from our research make it quite evident that *Magnifera indica* reduced edema and pain effects in our test animals, suggesting that it can be beneficial for human beings as well if used. More studies are needed to assess the pharmacological activity of Mangifera indica further and the role of its chemical constituents in different diseases.

CONCLUSION

Since ages, *Mangifera indica* has been evaluated for its beneficial pharmacological activity. The hot plate method, tail flick test, and writhing test are techniques for assessing analgesic activity. In our current study, the extract has shown significant analgesic effects in animal models. However, more investigations are required to detect the active chemical substances involved in analgesic characteristics.

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DECLARATIONS

Authors' contributions

IJ conceptualized and drafted the manuscript. SHAZ and MF compiled the data. SBZ did data analysis and interpretation. SA did a literature study and critical review of the manuscript. All the authors read and approved the final manuscript.

Ethical approval

The Ethical Committee on Research at the University of Karachi approved the study (reference No. 04178/Pharm).

Conflict of interest

The authors declared no conflict of interest among them.

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Data availability statement

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

REFERENCES

1. Moayedi M, Davis KD. Theories of pain: from specificity to gate control. Journal of Neurophysiology. 2013;109:5-12. https://doi.org/10.1152/jn.00457.2012.

2. Yong RJ, Mullins PM, Bhattacharyya N. Prevalence of chronic pain among adults in the United States. Pain. 2022;163:e328-e332. https://doi.org/10.1097/j.pain.0000000000002291

3. Bennett MI, Kaasa S, Barke A, Korwisi B, Rief W, Treede RD. The IASP classification of chronic pain for ICD-11: chronic cancer-related pain. Pain. 2019;160:38-44. https://doi.org/10.1097/j.pain.0000000000001363

4. Harvey RA, Clark M, Finkel R, Rey J, Whalen K. Lippincott's illustrated reviews. Pharmacology. 2012;526:530-541.

5. Joseph L, Cuerrier A, Mathews D. Shifting narratives, recognizing resilience: new anti-oppressive and decolonial approaches to ethnobotanical research with indigenous communities in Canada. Botany. 2022;100:65-81. https://doi.org/10.1139/cjb-2021-0111.

6. Shah KA, Patel MB, Patel RJ, Parmar PK. *Mangifera indica* (mango). Pharmacognosy Reviews. 2010;4:42-48. https://doi.org/10.4103/0973-7847.65325.

7. Kumar M, Saurabh V, Tomar M, Hasan M, Changan S, Sasi M, Maheshwari C, Prajapati U, Singh S, Prajapat RK, Dhumal S. Mango (*Mangifera indica L.*) leaves: Nutritional

composition, phytochemical profile, and health-promoting bioactivities. Antioxidants. 2021;10:299. https://doi.org/10.3390/antiox10020299.
8. Dereje B, Abera S, Effect of pretreatments and drying methods on the quality of dried mango (*Mangifera indica L.*) slices. Cogent Food and Agriculture. 2020;6:1747961. https://doi.org/10.1080/23311932.2020.1747961.
9. Alaiya MA, Odeniyi MA. Utilization of *Mangifera indica* plant extracts and parts in antimicrobial formulations and as a pharmaceutical excipient: a review. *Future* Journal of Pharmaceutical Sciences. 2023;9:29. https://doi.org/10.1186/s43094-023-00479-z.
10. Salimi Y, Tavahodi N, Taheri H, Masoudi M, Modaber MS, Azimi N, ... & Deravi, N. Effect of Mangifera Indica (Mango) on Dental Caries: A Systematic Review. Nutrition and Metabolic Insights. 2023;16: 11786388231204200. https://doi.org/ 10.1177/11786388231204200.
11. Council NR, Guide for the care and use of laboratory animals. National Academy Press, Washington, pp 1–7, (1996).
12. Hosseinzadeh H, Ramezani M, Salmani G. Anti-nociceptive, anti-inflammatory and acute toxicity effects of *Zataria* multiflora Boiss extracts in mice and rats. Journal of Ethnopharmacology. 2000;73:379-85. https://doi.org/10.1016/S0378-8741(00)00238-5.
13. Liyanagamage DS, Jayasinghe S, Attanayake AP, Karunaratne V. Acute and subchronic toxicity profile of a polyherbal drug used in Sri Lankan traditional medicine. Evidence-Based Complementary and Alternative Medicine. 2020. https://doi.org/10.1155/2020/2189189.
14. Tamrat Y, Nedi T, Assefa S, Teklehaymanot T, Shibeshi W. Anti-inflammatory and analgesic activities of solvent fractions of leaves of *Moringa stenopetalaBak*. (Moringaceae) in mice models, BMC Complementary Medicine and Therapeutics. 2017;17:473. https://doi.org/ 10.1186/s12906-017-1982-y.
15. Madhuri AS, Mohanvelu R, Ramabhimaiah S. Evaluation of anti-inflammatory activity of aqueous extract of *Mangifera indica* leaves in albino rats. International Journal of Basic and Clinical Pharmacology. 2016;5:635.
16. Tor PN, Gav BL, Saviour IM. The use of some plant-based natural preservatives in the preservation of mango fruits in benue state, Nigeria. American Journal of Innovation in Science and Engineering. 2016;2:76-92. https://doi.org/10.54536/ajise.v2i1.1306.
17. Zhou WS, Silva M, Yang C, Li S, Chen YT, Zheng WH. Mechanism and molecular targets of a water-soluble extract of *Artemisia annua* on the treatment of Alzheimer's disease based on network pharmacology and experimental validation. American Journal of Chinese Medicine. 2023;51:595-622. https://doi.org/10.1142/S0192415X23500295.
18. Pal SK, Shukla Y. Herbal medicine: Current status and the future. Asian Pacific Journal of Cancer Preventive. 2003;4:281-288.
19. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: Past history and future perspective. Journal of HerbMed Pharmacology. 2018;7:1-7.
20. Bentley GA, Newton SH, Starr J. Studies on the anti-nociceptive action of α-agonist drugs and their interactions with opioid mechanisms. British Journal of Pharmacology. 1983;79:125-134. https://doi.org/10.1111/j.1476 5381.1983.tb10504.x.
21. Alblihed MA. Astragalin attenuates oxidative stress and acute inflammatory responses in carrageenan-induced paw edema in mice. Molecular Biology Report. 2020;47:6611-6620. https://doi.org/10.1007/s11033-020-05712-z.
22. Du S, Liu H, Lei T, Xie X, Wang H, He X, ... & Wang Y. Mangiferin: An effective therapeutic agent against several disorders. Molecular Medicine Reports. 2018;18: 4775-4786. https://doi.org/10.3892/mmr.2018.9529.
23. Masibo M, He Q. Major mango polyphenols and their potential significance to human health,. Comprehensive Reviews in Food Science and Food Safety. 2008;7:309-319. https://doi.org/10.1111/j.15414337.2008.00047.x.
24. Saudagar RB, Saokar S. Anti-inflammatory natural compounds from herbal and marine

origin. Journal of Drug Delivery and Therapy. 2019;9:669-672. https://doi.org/10.22270/jddt.v9i3.2906.
25. Kaidama WM, Gacche RN. Anti-inflammatory activity of chrysin in acute and chronic phases of inflammation in Guinea Pigs. International Journal of Scientific and Research Publications. 2015;5:427-431.
26. Sayago-Ayerdi S, García-Martínez DL, Ramírez-Castillo AC, Ramírez-Concepción HR, Viuda-Martos M. Tropical fruits and their co-products as bioactive compounds and their health effects: A review. Foods. 2021;10:1952. https://doi.org/10.3390/foods10081952.